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(57) Abstract

N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is combined with cyclodextrin to form compositions exhibiting increased stability and solubility. Cyclodextrin can be α, β or γ, or a mixture thereof, and may be substituted or unsubstituted. This stabilized complex can be used in a variety of applications. Complex formation can be accomplished by a variety of methods, such as co-precipitation, slurry complexation, paste complexation, mixing and heating, extrusion, dry mixing, wet pelletization, agglomeration and other methods known in the art.

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TITLE

THE USE OF CYCLODEXTRIN TO STABILIZE N-[N-(3,3-DIMETHYLBUTYL)-1-α-ASPARTYL]-L-PHENYLALANINE 1-METHYL ESTER

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to a sweetener composition comprising N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (neotame) and cyclodextrin. The invention also relates to a process for stabilizing sweetener compositions. Further, this invention relates to a method of sweetening beverages, fluid dairy products, condiments, baked goods, frostings, bakery fillings, candies, chewing gum and table-top sweeteners, as well as to the compositions prepared by this method.

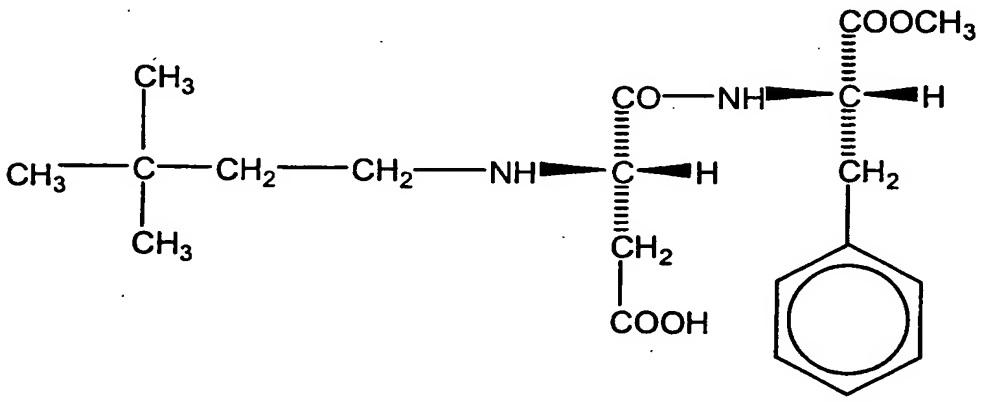
Related Background Art

U.S. Patent No. 5,070,081 describes a process of forming inclusion complexes of cyclodextrin via agglomeration. This patent discloses the use of such inclusion complexes, for among other things, foods, pharmaceuticals, cosmetics and agriculture. Also

disclosed are several advantages and uses of cyclodextrin complexes: controlled storage and release; improved physical and chemical stability of labile compounds; masking of off tastes or odors; enhanced bioavailability; stabilization of food flavors; easier tablet formation; separation, concentration and fractionation of substances. There is no disclosure or suggestion of cyclodextrin complexes of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

European Patent Application 0 097 950 relates to stabilized compositions comprising aspartame in an aqueous medium such as aqueous foods containing aspartame. The compositions further comprise a stabilizing agent (cyclodextrin, either alone or in combination with a sucrose fatty acid ester) which allows for long-term storage of the composition or food without significant deterioration of the aspartame. EP 0 097 950 indicates that cyclodextrin complexation is useful in increasing stability and solubility of aspartame.

N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (neotame) is a high potency dipeptide sweetener (about 8000X sweeter than sucrose) that has the formula



Although N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is a uniquely stable high potency sweetener, it may degrade when used in foods under certain conditions, such as high pH, high temperature, or in the presence of reactive co-ingredients. Of course, there is always a desire to extend the shelf life of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester containing products. The use of encapsulants or other technologies to increase stability and to extend the shelf life of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is limited by the applications in which they can be used, as well as by their effectiveness.

Cyclodextrin inclusion is a molecular phenomenon in which one or more guest molecules interacts with the cavity of one or more cyclodextrin molecules to become entrapped, unlike encapsulation in which more than one guest molecule is entrapped in an encapsulation matrix. In order to form a cyclodextrin complex, guest molecules must come into contact with cyclodextrin cavities to form stable associations. A variety of non-covalent forces, such as van der Waal forces, hydrophobic interactions and other forces, are responsible for the formation of a stable complex.

The entire disclosure of "Cyclodextrin Complexation" by MaryJane Buehne of Cerestar USA, Inc., which generally describes cyclodextrin complexation, is incorporated herein by reference.

SUMMARY OF THE INVENTION

Cyclodextrin can be used in combination with N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (neotame) to add increased stability, dissolution and solubility of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in various applications. Further, cyclodextrin, due to its formation of a molecular complex, provides the best opportunity for stabilization of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester than other, less specific methods, such as encapsulation. Cyclodextrin can be α, ß or γ, and may be substituted or unsubstituted. This complex can be used in a variety of applications. Complex formation can be accomplished by a variety of methods, such as co-precipitation, slurry complexation, paste complexation, mixing and heating, extrusion, dry mixing, or other methods known in the art.

There are several advantages to such a cyclodextrin-stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester: increased sweetener stability in a variety of applications and increased solubility and dissolution rate.

This invention is directed to a sweetener composition comprising N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester and cyclodextrin. The compositions of this invention can be used, for example, as a sweetener for incorporation in processed foods and beverages or as a table-top sweetener.

Preferably the sweetener composition comprises cyclodextrin which is selected from the group consisting of α-cyclodextrin, ß-cyclodextrin, γ-

cyclodextrin, or a mixture thereof. The cyclodextrin may be substituted or unsubstituted.

In another preferred embodiment, the sweetener composition has a molar ratio of cyclodextrin to N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in the range from about 200:1 to about 1:50. Preferably, the molar ratio of cyclodextrin to neotame is in the range from about 10:1 to about 1:4.

Without being bound to theory, it is believed that the composition of this invention may comprise N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester inclusion complexes of cyclodextrin.

It is also believed that the composition of this invention may comprise agglomerates of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester inclusion complexes of cyclodextrin.

This invention is also directed to compositions such as beverages, fluid dairy products, condiments, baked goods, frostings, bakery fillings, candy and chewing gum containing the sweetener composition of this invention in an amount effective to sweeten the composition, as well as to a method of making such compositions.

The invention also includes table-top sweeteners comprised of the sweetener composition of this invention.

The sweetener composition of this invention may comprise N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in combination with another high intensity or natural sweetener.

Yet another embodiment of the invention is directed to a process for stabilizing a sweetener composition comprising the step of contacting cyclodextrin with N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester to form a mixture. The invention also includes a process for stabilizing a sweetener composition comprising adding cyclodextrin to a composition containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. The process may also include the step of agitating the mixture sufficiently to cause interpenetration of the components and inclusion complex formation.

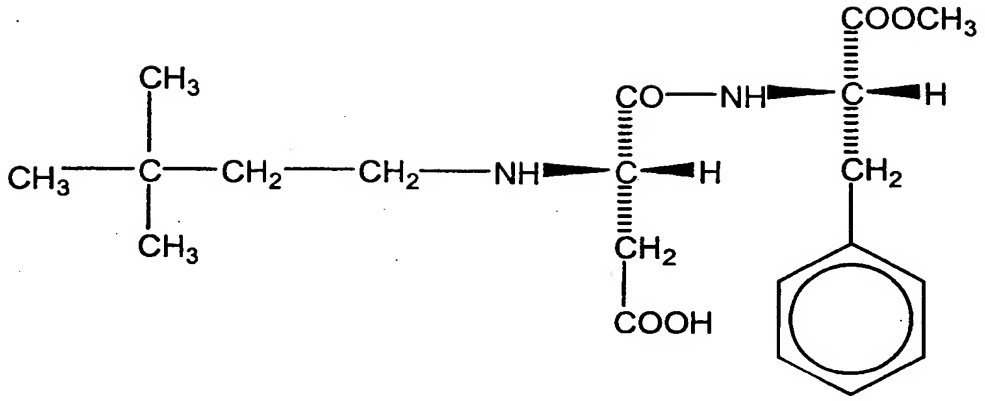
Methods used to stabilize the sweetener compositions of this invention include co-precipitation, slurry complexation, paste complexation, damp mixing and heating, extrusion, and dry mixing.

If desired, agitation may be continued until agglomerates form and then agglomerates of the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester inclusion complexes can be recovered.

Particularly preferred techniques include agglomeration and wet pelletization.

DETAILED DESCRIPTION

The N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (neotame) used in the present invention has the formula



The N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester may be prepared through various methods. One such method comprises the steps of (i) treating a mixture of aspartame and 3,3-dimethylbutyraldehyde in an organic solvent with hydrogen in the presence of a hydrogenation catalyst at a temperature and pressure effective to form an organic solvent solution of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester; (ii) filtering the organic solvent solution to remove the hydrogenation catalyst; and (iii) forming an aqueous/organic solvent solution from the organic solvent solution to precipitate the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester from the aqueous/organic solvent solution. Preferably, the aqueous/organic solvent solution has an amount of organic solvent of about 17% to about 30% by weight of the aqueous/organic solvent solution. A particularly preferred organic solvent for use in this method is methanol. The precipitate is recovered using standard filtration techniques to provide highly purified N-[N-3,3-dimethylbutyl)- L-α-aspartyl]-L-phenylalanine 1-methyl ester. This method of preparation is described in U.S. Patent No. 5,728,862, the entire disclosure of which is incorporated by reference herein. Further, the entire disclosures of U.S. Patents 5,480,668 and 5,510,508, also related to the synthesis and purification of N-[N-(3,3-

dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, are incorporated by reference herein.

The cyclodextrin used in the present invention is a cyclic oligosaccharide homolog that is also known as cycloamylose. It consists of 6 to 10 D-glucopyranose groups bonded through α-(1,4)-glucoside bonds to form a cyclic structure. It is named α-cyclodextrin, ß-cyclodextrin, or γ-cyclodextrin according to the degree of polymerization (6, 7 or 8 glucose units). The interior of the ring contains C-H bonds or ether bonds and is hydrophobic, while the exterior of the ring is interspersed with OH groups and is highly hydrophilic. Because of this structure, it is believed that cyclodextrin is capable of entrapping N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in its interior.

Cyclodextrin is usually produced from starch by treating it with an amylase or a similar enzyme produced from *Bacillus macerans* or an alkali-resistant bacterium. There are no particular limitations on the cyclodextrin that can be used in the present invention with respect to the conditions for producing it or other factors.

According to a preferred embodiment of the present invention, α-cyclodextrin, ß-cyclodextrin and γ-cyclodextrin may be used either independently or as a mixture, and either substituted or unsubstituted, although the intended object of the present invention may be achieved with any type of cyclodextrin. In particular, cyclodextrin may be substituted with alkyl, hydroxyalkyl, acetyl, amine, sulphate, or a mixture thereof. For example, dimethyl cyclodextrin, trimethyl cyclodextrin, tertiary amine cyclodextrin, carboxymethyl cyclodextrin, acetylated cyclodextrin,

hydroxypropyl cyclodextrin, hydroxyethyl cyclodextrin and sulphated cyclodextrin may be suitable for use in the present invention.

Stabilization of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester may be effected through simply using it together with the cyclodextrin, i.e., adding cyclodextrin to a composition containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. However, increased solubility and dissolution are better attained using a complexation technique.

Several techniques and variations thereof can be used to form N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester inclusion complexes of cyclodextrin. Factors such as the amount of complex to be formed, limitations imposed by the stability of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, and ease of recovery of the complex determine the plausibility of using individual techniques.

Co-precipitation is one method. According to this method, cyclodextrin is dissolved in water, and the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is added with stirring. The concentration of cyclodextrin is limited by the fact that N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester can tolerate higher temperatures for only a short time. Higher concentrations can be achieved, however, with more soluble cyclodextrin. Certain substituted cyclodextrins tend to have greater solubility. The concentration is chosen to be sufficiently high so that the solubility of the cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex will be exceeded as the complexation

reaction proceeds or as the reaction cools. The molar ratio of cyclodextrin to neotame is generally in the range of about 200:1 to about 1:50. Preferably, this range is from about 10:1 to about 1:4. The temperature range is not critical but generally is from about 35°C to about 80°C. Preferably, the temperature does not go above 80°C. Typically, the cyclodextrin complex is retrieved by collection of precipitate after cooling or by freeze drying.

The precipitate formed can be collected by decantation, centrifugation or filtration. The precipitate may be washed with a small amount of water or other water miscible solvent such as cold ethyl alcohol, cold methanol or cold acetone.

In addition to co-precipitation, it is contemplated that slurry complexation, paste complexation, damp mixing and heating, extrusion and dry mixing techniques can also be used to form the sweetener compositions of the present invention. These methods are outlined in "Cyclodextrin Complexation" by MaryJane Buehne of Cerestar USA, Inc.

Complexation may also be effected through an agglomeration method, such as that disclosed in U.S. Patent No. 5,070,081. Using this method, the cyclodextrin in solid form and the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester are contacted in the presence of a small amount of water sufficient to serve as an agglomeration binding liquid to form a mixture. Then the mixture is agitated sufficiently to cause interpenetration of the components and inclusion complex formation to occur. Agitation is continued until agglomerates form, and agglomerates are then recovered.

Wet pelletization techniques known in the art, including a severe agitation, may also be used to form agglomerates.

Only a portion of the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester molecule need fit into the cavity to form a complex, which is the case with many high molecular weight molecules. As a result, a one to one molar ratio is not always achieved.

Cyclodextrin is an expensive component, the use of which may result in flavor masking and other adverse conditions, such as off-taste notes or incompatability with other flavors, at high levels. However, because only minimal amounts of neotame are required for most applications, cyclodextrin need only be employed in relatively small amounts to stabilize the neotame according to the present invention. Thus, the use of cyclodextrin becomes cost-effective and the adverse effects of cyclodextrin at high levels are avoided.

The molar ratio of cyclodextrin to N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in the present invention ranges from about 200:1 to about 1:50. Preferably, the molar ratio of cyclodextrin to neotame is in the range from about 10:1 to about 1:4.

In the crystalline form, only the surface molecules of the cyclodextrin crystal are available for complexation. In solution, more cyclodextrin molecules become available for complexation. Heating increases the solubility of the cyclodextrin as well as that of the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. This increases the probability that a N-[N-(3,3-dimethylbutyl)-L-α-

aspartyl]-L-phenylalanine 1-methyl ester molecule and a cyclodextrin molecule will be able to come together to form a complex.

Temperature has more than one effect upon cyclodextrin complexes of this invention. While heating can increase the solubility of these complexes, it can also destabilize the complexes. Accordingly, it is necessary many times to balance these effects in preparation of the complexes of this invention. One of ordinary skill in the art can readily determine such a balance without undue experimentation.

Thus, heating may be used to form the complexes of this invention. Heat can be used to increase the solubility of the cyclodextrin and the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester to put individual molecules into solution so that the complexes of this invention can be formed. This temperature is generally in the range of 35°-80°C.

Cooling of the solution is usually necessary to crystallize or precipitate the complexes in order to allow formation of a stable complex and to decrease the solubility of this soluble complex. The solution is generally cooled to a temperature in the range of 0°-10°C. It is important to note that it may be desirable to leave some complex in solution, as opposed to completely crystallizing all complex out of solution, when recovering the inclusion complexes of the present invention.

The solvent of choice should be a solvent which does not complex well with cyclodextrin, which is easily removed, for example, by evaporation and in which N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is highly soluble so that only a small

amount of solvent is required. Further, the more soluble the cyclodextrin is in the solvent, the more molecules that are available for complexation. Water, ethanol, diethyl ether, methanol and isopropanol are examples of suitable solvents. In the present invention, water is the most commonly used solvent.

To further solubilize the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in the cyclodextrin solution, a small amount of solvent may be added or the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester may be dispersed as a fine precipitate. In the latter case, a long stirring or complexation time may be needed, but complexation occurs more rapidly than if the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester were still in the form of large crystals.

As the amount of solvent is increased, the amount of cyclodextrin and the amount of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester that can be solubilized increases so that more of these molecules exist in a molecular form that provides for complexation. As the amount of solvent is increased further, the cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester may become sufficiently dilute so that they do not come into contact with each other as frequently as in a more concentrated solution. It is also desirable to keep the amount of solvent sufficiently low to exceed the solubility of the complex. A greater amount of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is released more readily from the complex in the soluble state than in the solid or precipitated state.

The size of agglomerates can be varied by controlling the amount of solvent added and to a lesser degree by controlling the agitation. Increasing the amount of solvent tends to increase the agglomerate size. Increasing the agitation tends to decrease the agglomerate size.

The amount of solvent added when forming agglomerates normally will be within about 10 to about 100% by weight based on the cyclodextrin, preferably about 25-50%. Added solvent has been found necessary for formation of the complex and for agglomeration.

The drying of the complexes of this invention should be carefully controlled to avoid the loss of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. Drying can be accomplished by a variety of methods. Oven drying, drum drying, fluid bed drying, spray drying, low temperature drying, freeze drying, etc., may be used.

Agglomerates of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester are very easily recovered, handled and utilized.

Once a complex of this invention has been formed and dried, it is very stable and will remain stable at ambient temperatures under dry conditions. Displacement of the complexed N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester by another guest or heating is required to release the complexed N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

If complete removal of free N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester from agglomerates is necessary, well-established routine

procedures such as spray drying, freeze drying and vacuum drying could be used.

The cyclodextrin stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester compositions of this invention can be analyzed by a variety of techniques. The method or methods selected depend upon the desired information (whether complexation has occurred, how much complexation has occurred, which portions of the molecules are involved in complexation, etc.).

Physical and chemical analysis of the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complexes can be performed using established analytical methods. Methods such as nuclear magnetic resonance spectroscopy (NMR), fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) may be used. Further, methods such as high pressure liquid chromatography (HPLC) may be used. Additionally, the absorbance and fluorescence characteristics of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester are altered by complexation with cyclodextrin, thereby indicating the availability of a variety of spectrometric methods for chemical analysis.

The compositions of this invention are suitable for use in any food to replace natural sweeteners, as well as other high intensity sweeteners, normally used as sweeteners. The term food as used herein includes, for example, beverages, fluid dairy products, condiments, baked goods, frostings, bakery fillings, candies and chewing gum.

Beverages include, without limitation, carbonated soft drinks, including cola, lemon-lime, root beer, heavy

citrus ("dew type"), fruit flavored and cream sodas; powdered soft drinks, as well as liquid concentrates such as fountain syrups and cordials; coffee and coffee-based drinks, coffee substitutes and cereal-based beverages; teas, including dry mix products as well as ready-to-drink teas (herbal and tea-leaf based); fruit and vegetable juices and juice flavored beverages as well as juice drinks, nectars, concentrates, punches and "ades"; sweetened and flavored waters, both carbonated and still; sport/energy/health drinks; alcoholic beverages plus alcohol-free and other low-alcohol products including beer and malt beverages, cider, and wines (still, sparkling, fortified wines and wine coolers); other beverages processed with heating (infusions, pasteurization, ultra high temperature, ohmic heating or commercial aseptic sterilization) and hot-filled packaging; and cold-filled products made through filtration or other preservation techniques.

Fluid dairy products include, without limitation, non-frozen, partially frozen and frozen fluid dairy products such as, for example, milks, ice creams, sorbets and yogurts.

Condiments include, without limitation, ketchup, mayonnaise, salad dressing, Worcestershire sauce, fruit-flavored sauce, chocolate sauce, tomato sauce, chili sauce, and mustard.

Baked goods include, without limitation, cakes, cookies, pastries, breads, donuts and the like.

Bakery fillings include, without limitation, low or neutral pH fillings, high, medium or low solids fillings, fruit or milk based (pudding type or mousse

type) fillings, hot or cold make-up fillings and non-fat to full-fat fillings.

The present invention is particularly effective for enhancing the stability of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in the above-named foods and beverages which are canned, bottled, pouched, packaged or otherwise packed in manners suitable for shipping and display at room temperature or in a chilled state.

This invention is also directed to a sweetened food composition, such as described above, containing an effective amount of the sweetener composition of this invention to sweeten the food composition. Determination of the amount of sweetener composition to be added to the food composition, in order to effectively sweeten the food composition, can be readily determined by one of ordinary skill in the art.

The sweetener composition of the present invention can be used as a table-top sweetener. The sweetener composition of the present invention can be used for this purpose alone or in combination with known bulking agents. Suitable bulking agents include, but are not limited to, dextrose, maltodextrin, lactose, inulin, polyols, polydextrose, cellulose and cellulose derivatives. A table-top sweetener comprising the present sweetener composition may also include any other ingredients commonly present in table-top sweeteners in order to tailor the taste of the product to a specific end use. A table-top sweetener comprising the present sweetener composition may take any known form. Suitable forms include, but are not limited to, sachets including the sweetener in powder or granular form, tablets, liquid sweeteners, and jar,

pouches, pocket or other forms in which the sweetener may be measured in, for example, spoon for spoon form.

The sweetener composition of this invention can also include known natural sweeteners as well as other high intensity sweeteners. Sweeteners that may be employed include, without limitation, aspartame, acesulfame-K, sucralose, saccharin, alitame, cyclamates, stevia derivatives, thaumatin, sucrose (liquid and granulated), high fructose corn syrup, high conversion corn syrup, crystalline fructose, glucose (dextrose), polyol sugar alcohols, invert sugar and mixtures thereof.

The Examples which follow are intended as an illustration of certain preferred embodiments of the invention, and no limitation of the invention is implied.

EXAMPLE 1

1:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

ß-cyclodextrin (34.02 g, 0.03 mol) was slurried in a solution of 350 ml water and 75 ml ethanol, and the solution was heated using a hot plate. Once the ß-cyclodextrin/water/ethanol solution reached 50°C (approximately 0.5 hr), a separate N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (10.95 g, 0.03 mol) solution dissolved in 75 ml of ethanol was added. The clear solution was allowed to cool to 40°C (approximately 0.5 hr) then vacuum distilled until 230 ml of condensate was collected (approximately .75 hr). The solution was cooled under atmospheric conditions to 3°C (approximately 10 min). No precipitate had formed, so the product was freeze

dried to collect complex. Sample was analyzed using differential scanning calorimetry and compared with DSC scans of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, ß-cyclodextrin, and a dry blend of ß-cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. The data indicated the formation of the desired complex.

EXAMPLE 2

2.5:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

ß-cyclodextrin (28.35 g, 0.025 mol) was slurried in a solution of 350 ml water and 75 ml ethanol, and the solution was heated using a hot plate. Once the ß-cyclodextrin/water/ethanol solution reached 50°C (approximately 1 hr), a separate N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (3.7846 g, 0.010 mol) solution dissolved in 75 ml of ethanol was added. The clear solution was allowed to cool to 45°C (approximately 20 min) then vacuum distilled (28" Hg) until 210 ml of condensate was collected (approximately 3 hr). The solution was cooled under atmospheric conditions to 8°C (approximately 10 min). Some precipitate had formed, but the product was freeze dried to collect complex. Sample was analyzed using differential scanning calorimetry and compared with DSC scans of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, ß-cyclodextrin, and a dry blend of ß-cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. The data indicated the formation of the desired complex.

EXAMPLE 3

5:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

ß-cyclodextrin (28.35 g, 0.025 mol) was slurried in a solution of 350 ml water and 75 ml ethanol, and the solution was heated using a hot plate. Once the ß-cyclodextrin/water/ethanol solution reached 53°C (approximately 0.5 hr), a separate N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (1.8923 g, 0.0052 mol) solution dissolved in 75 ml of ethanol was added. The clear solution was allowed to cool to 42°C (approximately 1 hr) then vacuum distilled (28" Hg) until a precipitate formed (approximately 2.5 hr), which was suspected to be uncomplexed cyclodextrin. The vacuum was discontinued, after 180 ml of condensate was collected. The solution was freeze dried to collect complex. Sample was analyzed using differential scanning calorimetry and compared with DSC scans of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, ß-cyclodextrin, and a dry blend of ß-cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. The data indicated formation of the desired complex.

EXAMPLE 4

10:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

ß-cyclodextrin (28.35 g, 0.025 mol) was slurried in a solution of 350 ml water and 75 ml ethanol, and the solution was heated using a hot plate. Once the ß-cyclodextrin/water/ethanol solution reached 50°C (approximately 40 min), a separate N-[N-(3,3-

dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (0.94615 g, 0.0026 mol) solution dissolved in 75 ml of ethanol was added. The clear solution was allowed to cool to 43°C (approximately 0.5 hr) then vacuum distilled (28" Hg) until a precipitate formed (approximately 3 hr). The vacuum was discontinued, after 140 ml of condensate was collected. The solution was freeze dried to collect complex. Sample was analyzed using differential scanning calorimetry and compared with DSC scans of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, ß-cyclodextrin, and a dry blend of ß-cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. The data indicated formation of the desired complex.

COMPARATIVE EXAMPLE 1

Carbonated Soft Drink Formulation Containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester

A carbonated soft drink was formulated by adding to 978.50 g of distilled water, in the order specified, 1.00 g sodium benzoate, 0.10 g N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, 3.20 g cola acid and 17.20 g cola flavor.

EXAMPLE 5

Carbonated Soft Drink Formulation Containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester with Cyclodextrin Added

A carbonated soft drink was formulated by adding to 978.20 g of distilled water, in the order specified, 1.00 g sodium benzoate, 0.10 g N-[N-(3,3-

dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester, 0.31 g cyclodextrin, 3.20 g cola acid and 17.20 g cola flavor.

EXAMPLE 6

Carbonated Soft Drink Formulation Containing Cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Mixture

A carbonated soft drink was formulated by adding to 978.20 g of distilled water, in the order specified, 1.00 g sodium benzoate, 0.408 g premix (comprised of 0.102 g N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester and 0.306 g cyclodextrin), 3.20 g cola acid and 17.20 g cola flavor.

EXAMPLE 7

Carbonated Soft Drink Formulation Containing 1:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

A carbonated soft drink was formulated by adding to 978.194 g of distilled water, in the order specified, 1.00 g sodium benzoate, 0.408 g 1:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex, 3.20 g cola acid and 17.20 g cola flavor.

EXAMPLE 8

Carbonated Soft Drink Formulation Containing 2.5:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

A carbonated soft drink was formulated by adding to 977.700 g of distilled water, in the order specified, 1.00 g sodium benzoate, 0.867 g 2.5:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex, 3.20 g cola acid and 17.20 g cola flavor.

EXAMPLE 9

Carbonated Soft Drink Formulation Containing 5:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

A carbonated soft drink was formulated by adding to 977.000 g of distilled water, in the order specified, 1.00 g sodium benzoate, 1.632 g 5:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex, 3.20 g cola acid and 17.20 g cola flavor.

EXAMPLE 10

Carbonated Soft Drink Formulation Containing 10:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

A carbonated soft drink was formulated by adding to 975.400 g of distilled water, in the order specified, 1.00 g sodium benzoate, 3.158 g 10:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex, 3.20 g cola acid and 17.20 g cola flavor.

COMPARATIVE EXAMPLE 2

Chewing Gum Formulation Containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester

Sorbitol powder (1661.6 g) was divided into two equal portions. To one portion, 525 g of lycasin was added. Into an Aaron Process Mixer, 945 g gum base was placed and heated to about 115°-140°C. Hand mixed with the other portion of sorbitol powder was 0.900 g N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. The speed on the mixer was set to #80 and the neotame/sorbitol mixture was gradually added. Then, the lycasin/sorbitol mixture, 210 g glycerin, 105 g mannitol and 52.5 g peppermint flavor were added in that order. The temperature control was shut off and the product left to sit for 10 minutes. The product was then divided into four equal portions and dusted with mannitol. Each portion was rolled with a rolling pin to a thickness of 0.2" (0.51 cm) and cut into 1.5" x 0.5" (3.81 cm x 1.27 cm) strips.

EXAMPLE 11

Chewing Gum Formulation Containing 1:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

Sorbitol powder (1658.87 g) was divided into two equal portions. To one portion, 525 g of lycasin was added. Into an Aaron Process Mixer, 945 g gum base was placed and heated to about 115°-140°C. Hand mixed with the other portion of sorbitol powder was 3.629 g 1:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex. The speed on the mixer was set to #80 and the neotame complex/sorbitol

mixture was gradually added. Then, the lycasin/sorbitol mixture, 210 g glycerin, 105 g mannitol and 52.5 g peppermint flavor were added in that order. The temperature control was shut off and the product left to sit for 10 minutes. The product was then divided into four equal portions and dusted with mannitol. Each portion was rolled with a rolling pin to a thickness of 0.2" (0.51 cm) and cut into 1.5" x 0.5" (3.81 cm x 1.27 cm) strips.

EXAMPLE 12

Chewing Gum Formulation Containing 10:1 Cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester Complex

Sorbitol powder (1634.29 g) was divided into two equal portions. To one portion, 525 g of lycasin was added. Into an Aaron Process Mixer, 945 g gum base was placed and heated to about 115°-140°C. Hand mixed with the other portion of sorbitol powder was 28.213 g 10:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex. The speed on the mixer was set to #80 and the neotame complex/sorbitol mixture was gradually added. Then, the lycasin/sorbitol mixture, 210 g glycerin, 105 g mannitol and 52.5 g peppermint flavor were added in that order. The temperature control was shut off and the product left to sit for 10 minutes. The product was then divided into four equal portions and dusted with mannitol. Each portion was rolled with a rolling pin to a thickness of 0.2" (0.51 cm) and cut into 1.5" x 0.5" (3.81 cm x 1.27 cm) strips.

Carbonated Soft Drink Stability of ß-Cyclodextrin Stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester

Several different carbonated soft drink (CSD) formulations containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester and cyclodextrin were prepared.

TABLE 1. Sample Identification.

control Comp. Ex. 1	N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester only
Ex. 5	cyclodextrin simply added to CSD formulation containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester
Ex. 6	cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester combined and then added to CSD formulation
Ex. 7	1:1 complex of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (Example 1) added to CSD formulation
Ex. 8	2.5:1 complex of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (Example 2) added to CSD formulation
Ex. 9	5:1 complex of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (Example 3) added to CSD formulation
Ex. 10	10:1 complex of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (Example 4) added to CSD formulation

Table 2 below shows that the long-term stability of the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester was improved by using ß-cyclodextrin.

TABLE 2.

	residual N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (%)				
	0 wk	1 wk	2 wk	4 wk	6 wk
Comp. Ex. 1	100	95.25	87.82	83.80	64.66
Ex. 5	100	92.53	90.32	82.39	73.42
Ex. 6	100	95.55	87.71	78.87	77.30
Ex. 7	100	90.63	87.61	76.30	69.71
Ex. 8	100	92.71	87.66	80.00	67.54
Ex. 9	100	90.44	86.14	76.86	70.16
Ex. 10	100	91.99	87.31	78.19	71.66

TABLE 2, continued

	residual N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (%)				
	8 wk	14 wk	16 wk	20 wk	26 wk
Comp. Ex. 1	58.17	47.26	40.09	36.95	25.44
Ex. 5	64.46	53.74	44.18	43.14	32.42
Ex. 6	69.03	51.97	43.26	47.84	34.11
Ex. 7	65.90	47.64	38.69	45.04	28.42
Ex. 8	66.38	50.15	43.53	46.87	29.24
Ex. 9	64.60	49.48	39.69	44.27	30.30
Ex. 10	65.13	51.45	42.58	45.35	31.67

Table 3 illustrates the increase in half life achieved by cyclodextrin stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. Table 3 was generated using the data from Table 2.

TABLE 3. Half Life.

	half life (weeks)	% increase v. control
Comp. Ex. 1	13.4	
Ex. 7	15.5	15.7
Ex. 8	15.5	15.7
Ex. 9	16.2	20.9
Ex. 10	16.7	24.6

Chewing Gum Stability of ß-Cyclodextrin Stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester

Three different chewing gum formulations containing N-[N-3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester and cyclodextrin were prepared.

TABLE 4. Sample Identification.

control Comp. Ex. 2	N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester only
Ex. 11	1:1 complex of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (Example 1) added to chewing gum formulation
Ex. 12	10:1 complex of cyclodextrin and N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (Example 4) added to chewing gum formulation

TABLE 5.

	residual N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester (%)			
	0 wk	2 wk	4 wk	8 wk
Comp. Ex. 2	100	62.93	37.42	14.5
Ex. 11	100	62.45	39.09	20.7
Ex. 12	100	73.38	48.97	24.7

The increase in half life achieved by cyclodextrin stablized in N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in chewing gum is illustrated in Table 6. The half life data was generated from the data in Table 5.

TABLE 6. Half Life (chewing gum)

	half life (weeks)	% increase v. control
Comp. Ex. 2	2.9	
Ex. 11	3.6	24.1%
Ex. 12	3.9	34.5%

Dissolution of Cyclodextrin Stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester

The dissolution rate of several complexes of this invention and a control set forth in Table 7 were compared. Table 8 illustrates the improved dissolution of cyclodextrin stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester. Samples were analyzed via absorbance at 258 mu.

TABLE 7. Sample Identification.

A control	0.0750 g N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester in 150 ml water at 20°C
B	0.2250 g 1:1 N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester/cyclodextrin complex in 150 ml water at 20°C
C	0.3000 g 1:2.5 N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester/cyclodextrin complex in 150 ml water at 20°C
D	0.2812 g 1:5 N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester/cyclodextrin complex in 150 ml water at 20°C
E	0.1406 g 1:10 N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester/cyclodextrin complex in 150 ml water at 20°C

TABLE 8.

time (s)	A % dissolved	B % dissolved	C % dissolved	D % dissolved	E % dissolved
0	0	0	0	0	0
25	37	102	92	107	126
50	51	100	97	102	103
75	60	100	98	102	101
100	67	100	102	101	100
125	72	100	99	100	97
150	77	100	99	102	98
175	80	100	100	101	98
200	83	100	99	101	98
225	86	100	100	101	98
250	88	100	100	101	99
275	99	100	100	100	99
300	91	100	100	101	98
325	93	100	100	101	100
350	94	99	99	101	98
375	95	100	99	100	98
400	96	100	99	100	99
425	97	100	99	100	99
450	97	100	99	100	99
475	98	100	100	100	100
500	99	100	100	100	99
525	94	100	99	100	101
550	99	94	99	100	99
575	100	100	100	100	100
600	100	100	99	100	100

Note: ß-cyclodextrin has an interfering peak at 258 mu. With the samples that have higher concentrations of ß-cyclodextrin, there is an initial disturbance early in the absorbance pattern.

Solubility of Cyclodextrin Stabilized N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester

Water (25 ml) at room temperature was added to each of two 50 ml beakers. Uncomplexed neotame was added to the first beaker until the solution was cloudy and supersaturated. 1:1 cyclodextrin/N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester complex was added to the second beaker until the solution was cloudy and supersaturated. The solutions were allowed to reach equilibrium under continuous agitation over the course of four hours. Agitation was terminated, and the particulates that were not in solution were allowed to settle for a period of one half hour. Samples were drawn from the clear liquid at the top of each beaker and analyzed via HPLC. The solubility for uncomplexed neotame was 1.26865 g/100 ml water. The solubility for the 1:1 complex was 2.95476 g/ 100 ml water.

Other variations and modifications of this invention will be obvious to those skilled in this art. This invention is not to be limited except as set forth in the following claims.

What is claimed is:

1. A sweetener composition comprising N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester and cyclodextrin.

2. The sweetener composition according to claim 1, wherein the cyclodextrin is α-cyclodextrin, ß-cyclodextrin, γ-cyclodextrin, or a mixture thereof, and wherein the cyclodextrin is substituted or unsubstituted.

3. The sweetener composition according to claim 2 wherein the cyclodextrin is substituted and wherein the substituent is selected from the group consisting of alkyl, hydroxyalkyl, acetyl, amine, sulphate, and a mixture thereof.

4. The sweetener composition according to claim 1, wherein the molar ratio of cyclodextrin to N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is from 200:1 to 1:50.

5. The sweetener composition according to claim 4, wherein the molar ratio of cyclodextrin to N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester is from 10:1 to 1:4.

6. The sweetener composition according to claim 1, further comprising another high intensity sweetener, natural sweetener, or mixture thereof.

7. The sweetener composition according to claim 6, wherein said high intensity sweetener or said natural sweetener is selected from the group consisting of aspartame, acesulfame-K, sucralose, saccharin, alitame, cyclamates, stevia derivatives, thaumatin, sucrose

(liquid and granulated), high fructose corn syrup, high conversion corn syrup, crystalline fructose, glucose (dextrose), polyol sugar alcohols, invert sugar and mixtures thereof.

8. The sweetener composition according to claim 1, wherein the composition comprises N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester inclusion complexes of cyclodextrin.

9. A method of sweetening a beverage by including in said beverage a sweetener composition according to claim 1 in an amount effective to sweeten said beverage.

10. The method according to claim 9, wherein said beverage is selected from the group consisting of carbonated soft drinks, powdered soft drinks, coffees, teas, juices, sweetened and flavored waters, sport/energy/health drinks, alcoholic beverages, beverages processed with heating and hot-filled packaging and cold-filled beverages.

11. A method of sweetening a fluid dairy product by including in said fluid dairy product a sweetener composition according to claim 1 in an amount effective to sweeten said fluid dairy product.

12. The method according to claim 11, wherein said fluid dairy product is selected from the group consisting of non-frozen, partially frozen and frozen milks, ice creams, sorbets and yogurts.

13. A method of sweetening a condiment by including in said condiment a sweetener composition according to claim 1 in an amount effective to sweeten said condiment.

14. The method according to claim 13, wherein said condiment is selected from the group consisting of ketchup, mayonnaise, salad dressing, Worcestershire sauce, tomato sauce, chili sauce, and mustard.

15. A method of sweetening a baked good by including in said baked good a sweetener composition according to claim 1 in an amount effective to sweeten said baked good.

16. The method according to claim 15, wherein said baked good is selected from the group consisting of cakes, cookies, pastries, breads and donuts.

17. A method of sweetening a frosting by including in said frosting a sweetener composition according to claim 1 in an amount effective to sweeten said frosting.

18. A method of sweetening a bakery filling by including in said bakery filling a sweetener composition according to claim 1 in an amount effective to sweeten said bakery filling.

19. The method according to claim 18, wherein said bakery filling is a low or neutral pH filling, a high, medium or low solids filling, a fruit or milk based filling, a hot or cold make-up filling and a non-fat to full-fat filling.

20. A method of sweetening candy or chewing gum by including in said candy or chewing gum a sweetener composition according to claim 1 in an amount effective to sweeten said candy or chewing gum.

21. A method of sweetening a table-top sweetener by including in said table-top sweetener a sweetener

composition according to claim 1 in an amount effective to sweeten said table-top sweetener.

22. A sweetened beverage comprising a sweetener composition according to claim 1 in an amount effective to sweeten the beverage composition.

23. The sweetened beverage according to claim 22, wherein said beverage is selected from the group consisting of carbonated soft drinks, powdered soft drinks, coffees, teas, juices, sweetened and flavored waters, sport/energy/health drinks, alcoholic beverages, beverages processed with heating and hot-filled packaging and cold-filled beverages.

24. A sweetened fluid dairy product comprising a sweetener composition according to claim 1 in an amount effective to sweeten said fluid dairy product composition.

25. The sweetened fluid dairy product according to claim 24, wherein said fluid dairy product is selected from the group consisting of non-frozen, partially frozen and frozen milks, ice creams, sorbets and yogurts.

26. A sweetened condiment comprising a sweetener composition according to claim 1 in an amount effective to sweeten said condiment composition.

27. The sweetened condiment according to claim 26, wherein said condiment is selected from the group consisting of ketchup, mayonnaise, salad dressing, Worcestershire sauce, tomato sauce, chili sauce, and mustard.

28. A sweetened baked good comprising a sweetener composition according to claim 1 in an amount effective to sweeten said baked good.

29. The sweetened baked good according to claim 28, wherein said baked good is selected from the group consisting of cakes, cookies, pastries, breads and donuts.

30. A sweetened frosting comprising a sweetener composition according to claim 1 in an amount effective to sweeten said frosting.

31. A sweetened bakery filling comprising a sweetener composition according to claim 1 in an amount effective to sweeten said bakery filling.

32. The sweetened bakery filling according to claim 31, wherein said bakery filling is a low or neutral pH filling, a high, medium or low solids filling, a fruit or milk based filling, a hot or cold make-up filling and a non-fat to full-fat filling.

33. A sweetened candy or chewing gum comprising a sweetener composition according to claim 1 in an amount effective to sweeten said candy or chewing gum composition.

34. A table-top sweetener comprising a sweetener composition according to claim 1 in an amount effective to sweeten said table-top sweetener.

35. A process for stabilizing a sweetener composition comprising adding cyclodextrin to a composition containing N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

36. A process for stabilizing a sweetener composition comprising the step of:

a) contacting cyclodextrin with N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester to form a mixture.

37. The process for stabilizing a sweetener composition according to claim 36 further comprising the step of:

b) agitating the mixture sufficiently to cause inclusion complex formation.

38. The process for stabilizing a sweetener composition according to claim 37, wherein said process includes a method selected from the group consisting of co-precipitation, slurry complexation, paste complexation, damp mixing and heating, extrusion, and dry mixing.

39. The process for stabilizing a sweetener composition according to claim 37 further comprising the steps of:

c) continuing agitation until agglomerates form; and

d) recovering agglomerates of the N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester inclusion complexes.

40. The process for stabilizing a sweetener composition according to claim 39, wherein said process includes a method selected from the group consisting of agglomeration and wet pelletization.

41. The process for stabilizing a sweetener composition according to claim 39, wherein a solvent is added in an amount from about 10% to about 100% by weight based on the amount of cyclodextrin.

42. The process for stabilizing a sweetener composition according to claim 41, wherein a solvent is added in an amount from about 25% to about 50% by weight based on the amount of cyclodextrin.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/21471

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A23L 1/236
US CL :426/548
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 426/3, 548, 580, 590, 650, 658, 659, 660

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,070,081 A (MAJID ET AL.) 03 December 1991, entire document.	1-42
Y	US 5,480,668 A (NOFRE ET AL.) 02 January 1996, entire document.	1-42
Y	EP 0,097,950 A (OJIMA ET AL.) 01 November 1984, entire document.	1-42

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
06 DECEMBER 1999

Date of mailing of the international search report
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